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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/693,754	10/20/2000	Neil Berinstein	13115	7885

7590 03/12/2003

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EXAMINER
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ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 03/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/693,754	Applicant(s) Berinstein
	Examiner Anne Marie Wehbé	Art Unit 1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Dec 23, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-19* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/2/03 has been entered. As requested, the amendment filed after-final on 5/7/02 has been entered. Claims 1-19 are pending in the instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in the instant action can be found in the previous office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-16 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 4-16 depend ultimately on claim 1. Claim 1 has been amended to recite

methods of inducing an immune response to a tumor antigen in an animal comprising a priming step wherein a tumor antigen is administered in a first form to a lymphatic site, and a boosting step wherein the tumor antigen is administered in a second form to a lymphatic site. Amended claim 1 does not provide any antecedent basis for "the nucleic acid" recited in claims 4-16.

Claim Rejections - 35 USC § 102

The rejection of claims 1-2, 4-14, and 16 under 35 U.S.C. 102(b) as being anticipated by Hurpin et al. is withdrawn in view of applicant's amendment to claim 1.

The rejection of claims 1-17 under 35 U.S.C. 102(a) as being anticipated by WO 99/02183, 1/21/99, hereafter referred to as Kundig et al. is withdrawn in view of applicant's amendment to claim 1.

Claims 1-4, 9-10, and 16-17 are newly rejected under 35 U.S.C. 102(a) as being anticipated by WO 99/30733, 6/24/99, hereafter referred to as Dalemans et al. The applicant claims methods of inducing an immune response to a tumor antigen in an animal comprising a priming step wherein a tumor antigen is administered in a first form to a lymphatic site, and a boosting step wherein the tumor antigen is administered in a second form to a lymphatic site. The

applicant further claims said methods wherein the tumor antigen is selected from a group which includes gp100 and wherein the tumor antigen is in the form of a nucleic acid.

Dalemans et al. teaches a prime boost strategy for generating immune responses comprising the administration of a nucleic acid encoding an antigen followed by the administration of protein antigen (Dalemans et al., page 28, claims 1-13, and page 29, claims 19-24). Dalemans et al. further teaches the administration of the nucleic acid and peptide to the spleen or to lymph tissue associated with the skin (Dalemans et al., page 12). In addition, Dalemans et al. teaches the administration of tumor antigens including gp100 (Dalemans et al., page 5). Thus, by teaching all the elements of the claims, Dalemans et al. anticipates the instant invention as claimed.

Claim Rejections - 35 USC § 103

The rejection of claims 1, and 17-19 under 35 U.S.C. 103(a) as being unpatentable over WO 99/02183, 1/21/99, hereafter referred to as Kundig et al, in view of Zaremba et al. and Salgaller et al., is withdrawn in view of applicant's amendments to claim 1.

Claims 1-2, 4-14, and 16-17 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Hurpin et al. (1998) Vaccine, Vol. 16 (2/3) 208-215, in view of Hodge et al. (1997) Vaccine, Vol. 15, No. 6/7, 759-768. The applicant claims methods of inducing an immune response to a tumor antigen in an animal comprising a priming step wherein a tumor antigen is

administered in a first form to a lymphatic site, and a boosting step wherein the tumor antigen is administered in a second form to a lymphatic site. The applicant further claims said methods wherein the tumor antigen is selected from a group which includes p53 and wherein the tumor antigen is in the form of a nucleic acid selected from a group which includes the canarypox nucleic acid, ALVAC.

Hurpin et al. teaches the generation of anti-53 CTL responses in mice following intrasplenic injection of ALVAC encoding p53 (Hurpin et al., page 209, column 2, second paragraph, and page 210, column 2, last paragraph, and page 211, Figure 1, panel b). While Hurpin et al. does not specifically teach a boosting step in addition to a priming step, Hurpin et al. does teach that the route of administration is also important for boosting the response (Hurpin et al., page 211, column 1, paragraph 1). Hodge et al. supplements Hurpin et al. by teaching a diversified prime and boost protocol for enhancing T-cell immunity and antitumor immune responses. Specifically, Hodge et al. teaches that priming an anti-tumor immune response by administering a vaccinia virus encoding CEA followed by boosting with an avipox virus (ALVAC) encoding CEA results in the generation of anti-CEA immune responses superior to those generated by the use of either vector alone (Hodge et al., page 759, and page 766, Table 3). Vaccinia virus encoding CEA and ALVAC encoding CEA represent different forms of the same tumor antigen since vaccinia is a cowpox virus and ALVAC is an avipox virus. Based on the motivation to use a diversified prime and boost strategy as taught by Hodge et al., and further based on the motivation to utilize intrasplenic injection for generating CTL using ALVAC

encoding tumor antigens as taught by Hurpin et al., it would have been *prima facie* obvious to the skilled artisan at the time of filing to administer a vaccinia virus encoding a tumor antigen, either CEA or p53, to the spleen followed by the intrasplenic administration of an avipox vector encoding either CEA or p53 in order to induce an immune response in an animal. Further, based on the successful use of intrasplenic administration to generate anti-tumor CTL as taught by Hurpin et al., and the successful use of a second vector to boost the immune response taught by Hodge, the skilled artisan would have had a reasonable expectation of success in induce an immune response in an animal by administering a vaccinia virus encoding a tumor antigen, either CEA or p53, to the spleen followed by the intrasplenic administration of an avipox vector encoding either CEA or p53.

In regards to applicant's argument that Hurpin et al. does not teach intrasplenic injection, the applicant is directed to page 209, column 2, second paragraph, and page 210, column 2, last paragraph, and page 211, Figure 1, panel b of Hurpin. In particular, please note that i.s. stands for intrasplenic.

Claims 1, and 17-19 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Hurpin et al. (1998) Vaccine, Vol. 16 (2/3) 208-215, in view of Hodge et al. (1997) Vaccine, Vol. 15, No. 6/7, 759-768, as applied to claims 1-2, 4-14, and 16-17 above, and further in view of Zaremba et al. (1997) Canc. Res., Vol. 57, 4570-4577 and Salgaller et al. (1996) Canc. Res., Vol. 56, 4749-4757. The applicant claims methods of inducing an immune response to a tumor antigen

in an animal comprising a priming step wherein a tumor antigen is administered in a first form to a lymphatic site, and a boosting step wherein the tumor antigen is administered in a second form to a lymphatic site. The applicant further claims said methods wherein the tumor antigen comprises the sequence YLSGADLNL or YLEPGPVTV.

Hurpin et al. in view of Hodge et al., as discussed in detail above, teach the use of a diversified prime and boost strategy which utilizes intrasplenic injection of a vaccinia virus encoding a tumor antigen, such as CEA or p53, followed by the intrasplenic administration of an avipox vector encoding a tumor antigen in order to induce an immune response in an animal. While Hurpin et al. and Hodge et al. teach the generation of anti-tumor immune responses against tumor antigens, including CEA, neither Hurpin et al. nor Hodge et al. teach wherein the tumor antigen comprises the sequence YLSGADLNL or YLEPGPVTV. Zaremba et al. supplements Hurpin and Hodge by teaching that the YLSGADLNL epitope is a CTL enhancer agonist peptide for inducing potent anti-CEA CTL (Zaremba et al., page 4570, abstract). Zaremba et al. further provides motivation for using the modified CEA peptide to induce anti-CEA CTL by teaching that the YLSGADLNL peptide is more potent that the unmodified YLSGANLNL peptide in inducing anti-CEA CTL (Zaremba et al., page 4574). Sangeller et al. further supplements Hurpin and Hodge by teaching a modified gp100 peptide YLEPGPVTV, which also demonstrates an enhanced ability to generate anti-gp100 CTL than the unmodified YLEPGPVTA peptide (Sangeller et al., page 4749, abstract and column 2). Thus, based on the motivation provided by Zaremba et al. and Sangeller et al. that the modified peptides YLSGADLNL and YLEPGPVTV

are more potent than the unmodified parent peptides at generating anti-CEA or anti-gp100 CTL respectively, it would have been *prima facie* obvious to the skilled artisan at the time of filing to substitute the modified YLSGADLNL or YLEPGPVTV peptides for the unmodified tumor antigens taught by Hurpin and Hodge, and further to use those peptides in the methods of Hurpin et al. in view of Hodge et al. for immunizing a mammal with a reasonable expectation of success.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (703) 306-9156. The examiner can be reached Mon-Fri from 10:30-7:00 EST. If the examiner is not available, the examiner's supervisor, Deborah Reynolds, can be reached at (703) 305-4051. General inquiries should be directed to the group receptionist whose phone number is (703) 308-0196. The technology center fax number is (703) 308-4242, the examiner's direct fax number is (703) 746-7024.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER